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Supplementary table S1: Summary of the genetic variants for BMI for the 73 BMI GRS

Trait	Genetic variant	Locus	Exclude from score	Reason for exclusion	Trait raising allele	Trait lowering allele	Imputation quality	Beta representing SD change in BMI from the primary GWAS*
BMI	rs1000940	<i>RABEP1</i>	No	NA	G	A	0.998767	0.019
BMI	rs10132280	<i>STXBP6</i>	No	NA	C	A	0.989184	0.023
BMI	rs1016287	<i>FLJ30838</i>	No	NA	T	C	0.998017	0.023
BMI	rs10182181	<i>ADCY3</i>	No	NA	G	A	0.99677	0.031
BMI	rs10733682	<i>LMX1B</i>	No	NA	A	G	0.966835	0.017
BMI	rs10938397	<i>GNPDA2</i>	No	NA	G	A	1	0.04
BMI	rs10968576	<i>LINGO2</i>	No	NA	G	A	1	0.025
				BMI-raising allele also associated with regular smoking (which itself has a causal effect on BMI in opposite direction)				
BMI	rs11030104	<i>BDNF</i>	Yes		A	G	0.99901	0.041
BMI	rs11057405	<i>CLIP1</i>	No	NA	G	A	1	0.031
BMI	rs11126666	<i>KCNK3</i>	No	NA	A	G	0.997088	0.021
BMI	rs11165643	<i>PTBP2</i>	No	NA	T	C	0.998186	0.022
BMI	rs11191560	<i>NT5C2</i>	No	NA	C	T	0.999813	0.031
BMI	rs11583200	<i>ELAVL4</i>	No	NA	C	T	0.994046	0.018
BMI	rs1167827	<i>HIP1</i>	No	NA	G	A	1	0.02
BMI	rs11688816	<i>EHBP1</i>	No	NA	G	A	0.993737	0.017
BMI	rs11727676	<i>HHIP</i>	No	NA	T	C	1	0.036
BMI	rs11847697	<i>PRKD1</i>	No	NA	T	C	1	0.049
BMI	rs12286929	<i>CADM1</i>	No	NA	G	A	0.997012	0.022
BMI	rs12401738	<i>FUBP1</i>	No	NA	A	G	0.995778	0.021
BMI	rs12429545	<i>OLFM4</i>	No	NA	A	G	0.982609	0.033
BMI	rs12446632	<i>GPRC5B</i>	No	NA	G	A	0.999769	0.04

BMI	rs12566985	<i>FPGT-TNNI3K</i>	No	NA	G	A	0.998568	0.024
BMI	rs12885454	<i>PRKD1</i>	No	NA	C	A	0.998387	0.021
BMI	rs12940622	<i>RPTOR</i>	No	NA	G	A	0.99906	0.018
BMI	rs13021737	<i>TMEM18</i>	No	NA	G	A	0.99987	0.06
BMI	rs13078960	<i>CADM2</i>	No	NA	G	T	0.994176	0.03

BMI	rs13107325	<i>SLC39A8</i>	Yes	Missense Ala/Thr polymorphism located in exon 7 of SLC39A8, which encodes a zinc transporter that also transports cadmium and manganese. It is also associated with BP and HDL levels, and presumably these and the BMI effect are secondary to the metal ion transport variation.		T	C	1	0.048
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BMI	rs13191362	<i>PARK2</i>	No	NA	A	G	0.995431	0.028
BMI	rs1516725	<i>ETV5</i>	No	NA	C	T	0.996107	0.045
BMI	rs1528435	<i>UBE2E3</i>	No	NA	T	C	0.997813	0.018
BMI	rs1558902	<i>FTO</i>	No	NA	A	T	0.999785	0.082
BMI	rs16851483	<i>RASA2</i>	No	NA	T	G	0.999167	0.048
BMI	rs16951275	<i>MAP2K5</i>	No	NA	T	C	0.999393	0.031
BMI	rs17001654	<i>SCARB2</i>	No	NA	G	C	0.976347	0.031
BMI	rs17024393	<i>GNAT2</i>	No	NA	C	T	0.99093	0.066
BMI	rs17094222	<i>HIF1AN</i>	No	NA	C	T	0.992428	0.025
BMI	rs17405819	<i>HNF4G</i>	No	NA	T	C	0.999855	0.022

BMI	rs17724992	PGPEP1	No	NA	A	G	0.991823	0.019	
BMI	rs1808579	C18orf8	No	NA	C	T	0.998227	0.017	
BMI	rs1928295	TLR4	No	NA	T	C	0.999945	0.019	
BMI	rs2033529	TDRG1	No	NA	G	A	0.992365	0.019	
BMI	rs2033732	RALYL	No	NA	C	T	1	0.019	
BMI	rs205262	C6orf106	No	NA	G	A	0.998614	0.022	
BMI	rs2075650	TOMM40	No	NA	A	G	1	0.026	
BMI	rs2112347	POC5	No	NA	T	G	1	0.026	
BMI	rs2121279	LRP1B	No	NA	T	C	0.992193	0.025	
BMI	rs2176598	HSD17B12	No	NA	T	C	1	0.02	
BMI	rs2207139	TFAP2B	No	NA	G	A	0.9998	0.045	
BMI	rs2245368	PMS2L11	No	NA	C	T	1	0.032	
BMI	rs2287019	QPCTL	No	NA	C	T	0.985702	0.036	
BMI	rs2365389	FHIT	No	NA	C	T	0.994976	0.02	
BMI	rs2650492	SBK1	No	NA	A	G	0.989836	0.021	
BMI	rs2820292	NAV1	No	NA	C	A	1	0.02	
BMI	rs29941	KCTD15	No	NA	G	A	1	0.018	
BMI	rs3101336	NEGR1	No	NA	C	T	1	0.033	
BMI	rs3736485	DMXL2	No	NA	A	G	0.995344	0.018	
BMI	rs3810291	ZC3H4	No	NA	A	G	1	0.028	
BMI	rs3817334	MTCH2	No	NA	T	C	1	0.026	
BMI	rs3849570	GBE1	No	NA	A	C	0.999768	0.019	
BMI	rs3888190	SH2B1	Yes	Associated with lots of other traits and is a big haplotype	A	C	0.999946	0.031	
BMI	rs4256980	TRIM66	No		NA	G	C	0.996389	0.021
BMI	rs4740619	C9orf93	No		NA	T	C	0.999082	0.018
BMI	rs543874	SEC16B	No		NA	G	A	1	0.048

BMI	rs6477694	<i>EPB41L4B</i>	No	NA	C	T	0.992092	0.017
BMI	rs6567160	<i>MC4R</i>	No	NA	C	T	0.998876	0.056
BMI	rs657452	<i>AGBL4</i>	No	NA	A	G	0.988962	0.023
BMI	rs6804842	<i>RARB</i>	No	NA	G	A	0.993341	0.019
BMI	rs7138803	<i>BCDIN3D</i>	No	NA	A	G	1	0.032
BMI	rs7141420	<i>NRXN3</i>	No	NA	T	C	0.988677	0.024
BMI	rs7243357	<i>GRP</i>	No	NA	T	G	0.9922	0.022
BMI	rs758747	<i>NLRC3</i>	No	NA	T	C	0.979448	0.023
BMI	rs7599312	<i>ERBB4</i>	No	NA	G	A	0.981254	0.022
BMI	rs7899106	<i>GRID1</i>	No	NA	G	A	0.990754	0.04
BMI	rs9400239	<i>FOXO3</i>	No	NA	C	T	0.995847	0.019
BMI	rs9581854	<i>MTIF3</i>	No	NA	T	C	0.996839	0.03
BMI	rs9925964	<i>KAT8</i>	No	NA	A	G	0.998274	0.019

Supplementary Table S2: Summary of the results from the multiple methods of Mendelian randomisation in Caucasian individuals.

A. Linear and logistic regression, MR using 73 SNP BMI GRS

Supplementary table 2: Summary of the results from the multiple methods of Mendelian randomisation in Caucasian individuals.

			RESULTS FROM LINEAR AND LOGISTIC REGRESSION ANALYSES			RESULTS FROM 1-SAMPLE 73 SNP BMI GRS		
Outcome	Strata	Number	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women
Socioeconomic position measures								
Townsend deprivation index	All	377786	0.079 (0.076, 0.082)	<1x10 ⁻¹⁵		0.09 (0.06, 0.11)	4x10 ⁻¹²	
Townsend deprivation index	Men only	174144	0.049 (0.045, 0.054)	<1x10 ⁻¹⁵	<1x10 ⁻¹⁵	0.07 (0.03, 0.10)	0.0002	0.10
Townsend deprivation index	Women only	203642	0.104 (0.100, 0.108)	<1x10 ⁻¹⁵		0.11 (0.07, 0.14)	1x10 ⁻⁹	
Annual household income	All	326117	-0.073 (-0.077, -0.070)	<1x10 ⁻¹⁵		-0.08 (-0.10, -0.06)	4x10 ⁻⁷	
Annual household income	Men only	156521	-0.030 (-0.040, -0.020)	<1x10 ⁻¹⁵	<1x10 ⁻¹⁵	-0.05 (-0.09, -0.01)	0.006	0.21
Annual household income	Women only	169596	-0.113 (-0.118, -0.108)	<1x10 ⁻¹⁵		-0.09 (-0.12, -0.05)	9x10 ⁻⁶	
Years in education	All	374658	-0.100 (-0.103, -0.098)	<1x10 ⁻¹⁵		-0.04 (-0.07, -0.02)	0.001	
Years in education	Men only	172637	-0.108 (-0.112, -0.103)	<1x10 ⁻¹⁵	0.00003	-0.06 (-0.10, -0.03)	0.0003	0.07
Years in education	Women only	202021	-0.095 (-0.099, -0.090)	<1x10 ⁻¹⁵		-0.02 (-0.05, 0.02)	0.33	
Degree level education	All	374658	OR: 0.82 (0.81, 0.82)	<1x10 ⁻¹⁵		OR: 0.93 (0.89, 0.98)	0.0068	
Degree level education	Men only	172637	OR: 0.82 (0.81, 0.82)	<1x10 ⁻¹⁵	0.60	OR: 0.91 (0.85, 0.98)	0.012	0.45
Degree level education	Women only	202021	OR: 0.82 (0.81, 0.83)	<1x10 ⁻¹⁵		OR: 0.95 (0.88, 1.02)	0.17	
Have a skilled job	All	245138	OR: 0.87 (0.86, 0.88)	<1x10 ⁻¹⁵		OR: 0.89 (0.82, 0.96)	0.003	
Have a skilled job	Men only	117866	OR: 0.87 (0.86, 0.89)	<1x10 ⁻¹⁵	0.30	OR: 0.86 (0.77, 0.96)	0.01	0.49
Have a skilled job	Women only	127272	OR: 0.86 (0.85, 0.87)	<1x10 ⁻¹⁵		OR: 0.91 (0.82, 1.02)	0.10	
In employment	All	222288	OR: 0.92 (0.90, 0.85)	1x10 ⁻⁹		OR: 0.94 (0.78, 1.14)	0.56	
In employment	Men only	109002	OR: 0.99 (0.96, 1.02)	0.54	<1x10 ⁻¹⁵	OR: 0.95 (0.76, 1.19)	0.64	0.95
In employment	Women only	113286	OR: 0.81 (0.77, 0.84)	<1x10 ⁻¹⁵		OR: 0.94 (0.67, 1.31)	0.70	
Social contact measures								
Weekly visits from friends and family	All	375985	OR: 1.06 (1.05, 1.07)	<1x10 ⁻¹⁵		OR: 0.98 (0.92, 1.04)	0.43	
Weekly visits from friends and family	Men only	173165	OR: 1.08 (1.07, 1.09)	<1x10 ⁻¹⁵	7x10 ⁻⁵	OR: 0.97 (0.89, 1.05)	0.41	0.79
Weekly visits from friends and family	Women only	202820	OR: 1.04 (1.03, 1.06)	3x10 ⁻¹³		OR: 0.98 (0.89, 1.08)	0.74	
Weekly participation in leisure and social activities	All	377246	OR: 0.91 (0.90, 0.91)	<1x10 ⁻¹⁵		OR: 0.96 (0.91, 1.01)	0.10	
Weekly participation in leisure and social activities	Men only	173923	OR: 0.97 (0.96, 0.98)	1x10 ⁻¹⁰	<1x10 ⁻¹⁵	OR: 0.92 (0.85, 0.99)	0.027	0.16
Weekly participation in leisure and social activities	Women only	203323	OR: 0.86 (0.85, 0.87)	<1x10 ⁻¹⁵		OR: 0.99 (0.92, 1.07)	0.85	
Weekly confiding in close friend or relative	All	367216	OR: 0.96 (0.95, 0.96)	<1x10 ⁻¹⁵		OR: 0.99 (0.93, 1.05)	0.63	
Weekly confiding in close friend or relative	Men only	168707	OR: 0.97 (0.96, 0.98)	2x10 ⁻⁷	3x10 ⁻⁵	OR: 1.00 (0.92, 1.08)	0.93	0.71
Weekly confiding in close friend or relative	Women only	198509	OR: 0.94 (0.93, 0.95)	<1x10 ⁻¹⁵		OR: 0.97 (0.89, 1.06)	0.57	
Cohabitation with partner or spouse	All	347329	OR: 0.98 (0.97, 0.99)	3x10 ⁻⁵		OR: 0.93 (0.87, 1.00)	0.043	
Cohabitation with partner or spouse	Men only	163873	OR: 1.04 (1.03, 1.05)	6x10 ⁻¹⁰	<1x10 ⁻¹⁵	OR: 1.07 (0.97, 1.17)	0.19	0.0004
Cohabitation with partner or spouse	Women only	183456	OR: 0.94 (0.93, 0.96)	<1x10 ⁻¹⁵		OR: 0.83 (0.76, 0.92)	0.0002	

*Difference in outcome is either reported as a SD difference for continuous traits or as an odds ratio (OR)

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B. Results from 942 SNP GRS, and results from 73 SNP IVW analysis

Supplementary table 2: Summary of the results from the multiple methods of Mendelian randomisation in Caucasian individuals.								
Outcome	Strata	Number	RESULTS FROM 1-SAMPLE 942 SNP BMI GRS			IVW RESULTS FROM 2-SAMPLE 73 BMI SNP		
Socioeconomic position measures			Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women
Townsend deprivation index	All	377786	0.08 (0.07, 0.10)	<1x10 ⁻¹⁵		0.07 (0.04, 0.11)	4x10 ⁻⁵	
Townsend deprivation index	Men only	174144	0.08 (0.06, 0.10)	5x10 ⁻¹³	0.32	0.06 (0.02, 0.10)	0.008	0.15
Townsend deprivation index	Women only	203642	0.09 (0.07, 0.11)	<1x10 ⁻¹⁵		0.09 (0.05, 0.13)	2x10 ⁻⁵	
Annual household income	All	326117	-0.10 (-0.11, -0.08)	<1x10 ⁻¹⁵		-0.04 (-0.08, -0.01)	0.02	
Annual household income	Men only	156521	-0.09 (-0.11, -0.07)	<1x10 ⁻¹⁵	0.48	-0.03 (-0.07, 0.01)	0.18	0.18
Annual household income	Women only	169596	-0.10 (-0.12, -0.08)	<1x10 ⁻¹⁵		-0.06 (-0.10, -0.01)	0.011	
Years in education	All	374658	-0.14 (-0.15, -0.13)	<1x10 ⁻¹⁵		-0.02 (-0.07, 0.02)	0.28	
Years in education	Men only	172637	-0.16 (-0.19, -0.13)	<1x10 ⁻¹⁵	0.020	-0.04 (-0.10, 0.01)	0.12	0.2
Years in education	Women only	202021	-0.13 (-0.15, -0.10)	<1x10 ⁻¹⁵		-0.01 (-0.06, 0.04)	0.80	
Degree level education	All	374658	OR: 0.77 (0.74, 0.79)	<1x10 ⁻¹⁵		OR: 0.94 (0.85, 1.04)	0.22	
Degree level education	Men only	172637	OR: 0.76 (0.73, 0.80)	<1x10 ⁻¹⁵	0.89	OR: 0.91 (0.82, 1.01)	0.09	0.25
Degree level education	Women only	202021	OR: 0.77 (0.74, 0.80)	<1x10 ⁻¹⁵		OR: 0.96 (0.86, 1.08)	0.51	
Have a skilled job	All	245138	OR: 0.76 (0.72, 0.80)	<1x10 ⁻¹⁵		OR: 0.90 (0.81, 0.99)	0.037	
Have a skilled job	Men only	117866	OR: 0.74 (0.69, 0.79)	<1x10 ⁻¹⁵	0.30	OR: 0.87 (0.77, 0.98)	0.024	0.26
Have a skilled job	Women only	127272	OR: 0.78 (0.73, 0.83)	7x10 ⁻¹⁵		OR: 0.92 (0.81, 1.04)	0.19	
In employment	All	222288	OR: 0.95 (0.85, 1.06)	0.33		OR: 0.97 (0.82, 1.14)	0.69	
In employment	Men only	109002	OR: 0.98 (0.86, 1.11)	0.72	0.41	OR: 0.99 (0.81, 1.21)	0.93	0.34
In employment	Women only	113286	OR: 0.88 (0.73, 1.07)	0.22		OR: 0.91 (0.66, 1.27)	0.59	
Social contact measures								
Weekly visits from friends and family	All	375985	OR: 1.08 (1.04, 1.12)	5x10 ⁻⁵		OR: 0.98 (0.91, 1.06)	0.64	
Weekly visits from friends and family	Men only	173165	OR: 1.06 (1.01, 1.11)	0.02	0.31	OR: 0.97 (0.89, 1.07)	0.58	0.39
Weekly visits from friends and family	Women only	202820	OR: 1.10 (1.04, 1.16)	0.001		OR: 0.99 (0.90, 1.09)	0.83	
Weekly participation in leisure and social activities	All	377246	OR: 0.88 (0.85, 0.90)	<1x10 ⁻¹⁵		OR: 0.96 (0.90, 1.04)	0.32	
Weekly participation in leisure and social activities	Men only	173923	OR: 0.90 (0.86, 0.94)	4x10 ⁻⁶	0.11	OR: 0.93 (0.85, 1.01)	0.08	0.17
Weekly participation in leisure and social activities	Women only	203323	OR: 0.86 (0.82, 0.89)	3x10 ⁻¹²		OR: 0.99 (0.91, 1.09)	0.91	
Weekly confiding in close friend or relative	All	367216	OR: 0.96 (0.93, 0.99)	0.017		OR: 0.98 (0.92, 1.05)	0.64	
Weekly confiding in close friend or relative	Men only	168707	OR: 0.98 (0.94, 1.02)	0.36	0.23	OR: 0.99 (0.91, 1.08)	0.83	0.44
Weekly confiding in close friend or relative	Women only	198509	OR: 0.94 (0.90, 0.99)	0.013		OR: 0.98 (0.89, 1.07)	0.67	
Cohabitation with partner or spouse	All	347329	OR: 1.01 (0.97, 1.05)	0.57		OR: 0.95 (0.89, 1.03)	0.21	
Cohabitation with partner or spouse	Men only	163873	OR: 1.07 (1.01, 1.13)	0.016	0.005	OR: 1.05 (0.96, 1.15)	0.27	0.007
Cohabitation with partner or spouse	Women only	183456	OR: 0.97 (0.92, 1.02)	0.20		OR: 0.89 (0.80, 0.98)	0.024	
*Difference in outcome is either reported as a SD difference for continuous traits or as an odds ratio (OR)								

C. MR Egger and Median IV results

Supplementary table 2: Summary of the results from the multiple methods of Mendelian randomisation in Caucasian individuals.

			MR EGGER RESULTS FROM 2-SAMPLE 73 BMI SNP				MEDIAN IV RESULTS FROM 2-SAMPLE 73 BMI SNP		
Outcome	Strata	Number	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women	Egger intercept p-value	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women
Socioeconomic position measures									
Townsend deprivation index	All	377786	0.02 (-0.06, 0.10)	0.62		0.15	0.05 (0.01, 0.09)	0.012	
Townsend deprivation index	Men only	174144	0.01 (-0.08, 0.11)	0.8	0.39	0.35	0.02 (-0.03, 0.08)	0.38	0.10
Townsend deprivation index	Women only	203642	0.03 (-0.07, 0.12)	0.57		0.15	0.07 (0.02, 0.12)	0.004	
Annual household income	All	326117	0.02 (-0.07, 0.11)	0.67		0.13	-0.04 (-0.08, 0.00)	0.06	
Annual household income	Men only	156521	0.04 (-0.06, 0.15)	0.43	0.29	0.15	-0.01 (-0.07, 0.05)	0.28	0.25
Annual household income	Women only	169596	-0.002 (-0.11, 0.10)	0.96		0.27	-0.004 (-0.10, 0.01)	0.14	
Years in education	All	374658	0.10 (-0.01, 0.21)	0.07		0.015	-0.002 (-0.04, 0.04)	0.92	
Years in education	Men only	172637	0.09 (-0.04, 0.22)	0.16	0.42	0.026	-0.01 (-0.07, 0.04)	0.66	0.20
Years in education	Women only	202021	0.11 (-0.01, 0.24)	0.07		0.036	0.02 (-0.03, 0.07)	0.51	
Degree level education	All	374658	OR: 1.38 (1.11, 1.72)	0.006		0.0004	OR: 1.00 (0.92, 1.08)	0.91	
Degree level education	Men only	172637	OR: 1.37 (1.08, 1.73)	0.011	0.47	0.0004	OR: 0.94 (0.84, 1.06)	0.33	0.06
Degree level education	Women only	202021	OR: 1.39 (1.07, 1.80)	0.016		0.003	OR: 1.06 (0.95, 1.17)	0.29	
Have a skilled job	All	245138	OR: 1.10 (0.86, 1.39)	0.46		0.079	OR: 0.93 (0.83, 1.04)	0.21	
Have a skilled job	Men only	117866	OR: 1.06 (0.79, 1.42)	0.7	0.38	0.14	OR: 0.86 (0.71, 1.04)	0.12	0.23
Have a skilled job	Women only	127272	OR: 1.13 (0.84, 1.52)	0.43		0.15	OR: 0.94 (0.81, 1.09)	0.41	
In employment	All	222288	OR: 1.17 (0.78, 1.76)	0.45		0.32	OR: 1.15 (0.89, 1.48)	0.29	
In employment	Men only	109002	OR: 1.41 (0.86, 2.32)	0.18	0.12	0.11	OR: 1.16 (0.85, 1.57)	0.36	0.17
In employment	Women only	113286	OR: 0.80 (0.35, 1.82)	0.60		0.74	OR: 0.87 (0.53, 1.43)	0.58	
Social contact measures									
Weekly visits from friends and family	All	375985	OR: 0.87 (0.72, 1.03)	0.12		0.13	OR: 0.98 (0.90, 1.08)	0.73	
Weekly visits from friends and family	Men only	173165	OR: 0.90 (0.72, 1.14)	0.38	0.31	0.48	OR: 1.08 (0.96, 1.22)	0.22	0.034
Weekly visits from friends and family	Women only	202820	OR: 0.83 (0.66, 1.03)	0.10		0.09	OR: 0.92 (0.81, 1.04)	0.18	
Weekly participation in leisure and social activities	All	377246	OR: 1.08 (0.90, 1.29)	0.41		0.18	OR: 0.99 (0.91, 1.09)	0.90	
Weekly participation in leisure and social activities	Men only	173923	OR: 0.98 (0.80, 1.21)	0.86	0.14	0.54	OR: 0.92 (0.81, 1.03)	0.14	0.06
Weekly participation in leisure and social activities	Women only	203323	OR: 1.16 (0.94, 1.44)	0.17		0.12	OR: 1.04 (0.93, 1.15)	0.53	
Weekly confiding in close friend or relative	All	367216	OR: 1.04 (0.89, 1.22)	0.62		0.46	OR: 0.99 (0.90, 1.08)	0.80	
Weekly confiding in close friend or relative	Men only	168707	OR: 1.13 (0.91, 1.39)	0.26	0.15	0.19	OR: 1.06 (0.94, 1.19)	0.34	0.06
Weekly confiding in close friend or relative	Women only	198509	OR: 0.96 (0.77, 1.21)	0.74		0.86	OR: 0.93 (0.82, 1.05)	0.24	
Cohabitation with partner or spouse	All	347329	OR: 0.96 (0.80, 1.14)	0.62		0.99	OR: 0.98 (0.90, 1.07)	0.67	
Cohabitation with partner or spouse	Men only	163873	OR: 0.97 (0.78, 1.21)	0.77	0.45	0.42	OR: 1.06 (0.94, 1.21)	0.34	0.20
Cohabitation with partner or spouse	Women only	183456	OR: 0.95 (0.74, 1.22)	0.71		0.55	OR: 0.98 (0.86, 1.11)	0.70	
*Difference in outcome is either reported as a SD difference for continuous traits or as an odds ratio (OR)									

*Difference in outcome is either reported as a SD difference for continuous traits or as an odds ratio (OR)

Supplementary Table S3. Adjustment of observational results for maternal smoking and birth weight

			Age and sex adjusted				Adjust for early life factors - maternal smoking and birth weight		
			RESULTS FROM LINEAR AND LOGISTIC REGRESSION ANALYSES				RESULTS FROM LINEAR AND LOGISTIC REGRESSION ANALYSES		
Outcome	Strata	Number	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women	Number	Difference in outcome (95% CI) per SD higher BMI*	P value	P compare men and women
			Socioeconomic position measures				Socioeconomic position measures		
Townsend deprivation index	All	377786	0.079 (0.076, 0.082)	<1x10-15		162932	0.074 (0.069, 0.079)	<1x10-15	
Townsend deprivation index	Men only	174144	0.049 (0.045, 0.054)	<1x10-15	<1x10-15	63932	0.043 (0.035, 0.051)	<1x10-15	<1x10-15
Townsend deprivation index	Women only	203642	0.104 (0.100, 0.108)	<1x10-15		99000	0.095 (0.089, 0.101)	<1x10-15	
Annual household income	All	326117	-0.073 (-0.077, -0.070)	<1x10-15		144484	-0.065 (-0.071, -0.060)	<1x10-15	
Annual household income	Men only	156521	-0.030 (-0.040, -0.020)	<1x10-15	<1x10-15	58931	-0.011 (-0.020, -0.003)	0.007	<1x10-15
Annual household income	Women only	169596	-0.113 (-0.118, -0.108)	<1x10-15		85553	-0.102 (-0.109, -0.096)	<1x10-15	
Years in education	All	374658	-0.100 (-0.103, -0.098)	<1x10-15		162042	-0.086 (-0.091, -0.081)	<1x10-15	
Years in education	Men only	172637	-0.108 (-0.112, -0.103)	<1x10-15	0.00003	63566	-0.092 (-0.100, -0.086)	<1x10-15	0.010
Years in education	Women only	202021	-0.095 (-0.099, -0.090)	<1x10-15		98476	-0.081 (-0.086, -0.075)	<1x10-15	
Degree level education	All	374658	OR: 0.82 (0.81, 0.82)	<1x10-15		162042	OR: 0.82 (0.82, 0.83)	<1x10-15	
Degree level education	Men only	172637	OR: 0.82 (0.81, 0.82)	<1x10-15	0.60	63566	OR: 0.82 (0.80, 0.83)	<1x10-15	0.18

Degree level education	Women only	202021	OR: 0.82 (0.81, 0.83)	<1x10-15		98476	OR: 0.83 (0.82, 0.84)	<1x10-15	
Have a skilled job	All	245138	OR: 0.87 (0.86, 0.88)	<1x10-15		113945	OR: 0.88 (0.86, 0.89)	<1x10-15	
Have a skilled job	Men only	117866	OR: 0.87 (0.86, 0.89)	<1x10-15	0.30	47287	OR: 0.87 (0.84, 0.89)	<1x10-15	0.23
Have a skilled job	Women only	127272	OR: 0.86 (0.85, 0.87)	<1x10-15		66658	OR: 0.88 (0.86, 0.90)	<1x10-15	
In employment	All	222288	OR: 0.92 (0.90, 0.85)	1x10-9		105851	OR: 0.93 (0.89, 0.97)	0.0007	
In employment	Men only	109002	OR: 0.99 (0.96, 1.02)	0.54	<1x10-15	44862	OR: 1.01 (0.96, 1.07)	0.59	2x10-6
In employment	Women only	113286	OR: 0.81 (0.77, 0.84)	<1x10-15		113286	OR: 0.83 (0.78, 0.88)	<1x10-15	
			Social support measures				Social support measures		
Weekly visits from friends and family	All	375985	OR: 1.06 (1.05, 1.07)	<1x10-15		162452	OR: 1.06 (1.05, 1.08)	<1x10-15	
Weekly visits from friends and family	Men only	173165	OR: 1.08 (1.07, 1.09)	<1x10-15	7x10-5	63711	OR: 1.08 (1.06, 1.10)	2x10-15	0.11
Weekly visits from friends and family	Women only	202820	OR: 1.04 (1.03, 1.06)	3x10-13		98741	OR: 1.05 (1.03, 1.07)	7x10-9	
Weekly participation in leisure and social activities	All	377246	OR: 0.91 (0.90, 0.91)	<1x10-15		162841	OR: 0.90 (0.89, 0.91)	<1x10-15	
Weekly participation in leisure and social activities	Men only	173923	OR: 0.97 (0.96, 0.98)	1x10-10	<1x10-15	63934	OR: 0.96 (0.95, 0.98)	4x10-5	<1x10-15
Weekly participation in leisure and social activities	Women only	203323	OR: 0.86 (0.85, 0.87)	<1x10-15		98907	OR: 0.86 (0.85, 0.87)	<1x10-15	
Weekly confiding in close friend or relative	All	367216	OR: 0.96 (0.95, 0.96)	<1x10-15		159619	OR: 0.96 (0.95, 0.97)	<1x10-15	
Weekly confiding in close friend or relative	Men only	168707	OR: 0.97 (0.96, 0.98)	2x10-7	3x10-5	62521	OR: 0.98 (0.96, 1.00)	0.019	0.0003

Weekly confiding in close friend or relative	Women only	198509	OR: 0.94 (0.93, 0.95)	<1x10-15		97098	OR: 0.94 (0.93, 0.96)	2x10-13	
Cohabitation with partner or spouse	All	347329	OR: 0.98 (0.97, 0.99)	3x10-5		148674	OR: 0.97 (0.96, 0.99)	0.0001	
Cohabitation with partner or spouse	Men only	163873	OR: 1.04 (1.03, 1.05)	6x10-10	<1x10-15	59926	OR: 1.04 (1.03, 1.07)	9x10-6	<1x10-15
Cohabitation with partner or spouse	Women only	183456	OR: 0.94 (0.93, 0.96)	<1x10-15		88748	OR: 0.93 (0.92, 0.95)	<1x10-15	

Supplementary Table S4: Associations between BMI and death of a partner/spouse or marital separation/divorce

Outcome	Individuals included	N Cases - controls	OR (95%CI) of outcome per SD higher BMI	P value
Divorce / marital separation in last 2 years	All	7,745 (339,536)	0.98 (0.96, 1.00)	0.03
Divorce / marital separation in last 2 years	Men only	4,047 (159,808)	1.02 (0.99, 1.05)	0.14
Divorce / marital separation in last 2 years	Women only	3,698 (179,728)	0.95 (0.92, 0.97)	2x10 ⁻⁵
Death of partner or spouse in last 2 years	All	4,415 (342,866)	1.05 (1.02, 1.07)	0.001
Death of partner or spouse in last 2 years	Men only	1,463 (162,392)	1.07 (1.02, 1.12)	0.004
Death of partner or spouse in last 2 years	Women only	2,952 (180,474)	1.03 (1.00, 1.07)	0.036

Supplementary Table S5: Association between BMI and cohabiting with a partner or spouse, stratified by age

Outcome	Individuals included	Age	N Cases - controls	Logistic regression OR (95%CI) of outcome per SD higher BMI	P value	Mendelian Randomization OR (95%CI) of outcome per SD higher BMI	P value
Cohabitation with a partner or spouse	All	<58 years	130,804 (28,934)	0.98 (0.97, 1.00)	0.014	0.89 (0.81, 0.98)	0.014
Cohabitation with a partner or spouse	Men only	<58 years	60,140 (14,004)	1.08 (1.06, 1.10)	4x10 ⁻¹⁵	1.07 (0.94, 1.21)	0.3
Cohabitation with a partner or spouse	Women only	<58 years	70,664 (14,930)	0.91 (0.89, 0.92)	2x10 ⁻²⁷	0.74 (0.64, 0.85)	1x10 ⁻⁵
Cohabitation with a partner or spouse	All	≥58 years	146,595 (40,996)	0.98 (0.97, 0.99)	0.0007	0.99 (0.90, 1.09)	0.88
Cohabitation with a partner or spouse	Men only	≥58 years	73,922 (15,807)	1.01 (0.99, 1.03)	0.31	1.08 (0.94, 1.24)	0.27
Cohabitation with a partner or spouse	Women only	≥58 years	72,673 (25,189)	0.96 (0.95, 0.98)	1x10 ⁻⁷	0.93 (0.81, 1.06)	0.27

Supplementary Table S6: Genetic associations between BMI and annual household income with and without adjustment for number of people living in the household

Individuals	Adjustment	N	RESULTS FROM LINEAR REGRESSION MODELS		RESULTS FROM 1-SAMPLE 73 SNP BMI GRS	
			Change in outcome (95% CI) per SD higher BMI*	P value	Change in outcome (95% CI) per SD higher BMI**	P value
All	Standard	326,117	-0.07 (-0.07, -0.06)	<1x10 ⁻¹⁵	-0.08 (-0.10, -0.06)	4x10 ⁻⁷
	Standard + number living in household	325,782	-0.06 (-0.07, -0.06)	<1x10 ⁻¹⁵	-0.06 (-0.09, -0.04)	4x10 ⁻⁶
Men only	Standard	156,521	-0.03 (-0.03, -0.02)	<1x10 ⁻¹⁵	-0.05 (-0.09, -0.01)	0.006
	Standard + number living in household	156,385	-0.03 (-0.03, -0.02)	<1x10 ⁻¹⁵	-0.05 (-0.09, -0.01)	0.006
Women only	Standard	169,596	-0.10 (-0.11, -0.10)	<1x10 ⁻¹⁵	-0.09 (-0.12, -0.05)	9x10 ⁻⁶
	Standard + number living in household	169,397	-0.10 (-0.10, -0.09)	<1x10 ⁻¹⁵	-0.07 (-0.11, -0.03)	0.0002

Supplementary Table S7: Observational and genetic associations between BMI and the different outcome measures in a subset of individuals with no known health problems.

			RESULTS FROM LINEAR AND LOGISTIC REGRESSION MODELS		RESULTS FROM 1-SAMPLE 73 SNP BMI GRS	
Outcome	Strata	Number	Change in outcome (95% CI) per SD higher BMI*	P value	Change in outcome (95% CI) per SD higher BMI**	P value
Socioeconomic position measures						
Townsend deprivation index	All	88,223	0.04 (0.03, 0.05)	<1x10 ⁻¹⁵	0.06 (0.01, 0.12)	0.031
Townsend deprivation index	Men only	41,222	0.007 (-0.003, 0.018)	0.17	0.03 (-0.05, 0.11)	0.44
Townsend deprivation index	Women only	47,001	0.07 (0.06, 0.08)	<1x10 ⁻¹⁵	0.09 (0.01, 0.17)	0.024
Annual household income	All	78,158	-0.03 (-0.04, -0.02)	2x10 ⁻¹⁴	-0.03 (-0.09, 0.03)	0.29
Annual household income	Men only	37,672	0.03 (0.02, 0.04)	1x10 ⁻⁶	-0.01 (-0.09, 0.07)	0.82
Annual household income	Women only	40,486	-0.08 (-0.09, -0.07)	<1x10 ⁻¹⁵	-0.05 (-0.14, 0.03)	0.22
Years in education	All	87,549	-0.09 (-0.10, -0.09)	<1x10 ⁻¹⁵	-0.02 (-0.08, 0.03)	0.42
Years in education	Men only	40,889	-0.10 (-0.11, -0.09)	<1x10 ⁻¹⁵	-0.03 (-0.11, 0.04)	0.38
Years in education	Women only	46,660	-0.09 (-0.09, -0.08)	<1x10 ⁻¹⁵	-0.01 (-0.09, 0.06)	0.74

Degree level education	All	87,549	OR: 0.82 (0.80, 0.83)	$<1 \times 10^{-15}$	OR: 0.93 (0.83, 1.05)	0.25
Degree level education	Men only	40,889	OR: 0.82 (0.80, 0.83)	$<1 \times 10^{-15}$	OR: 0.94 (0.79, 1.11)	0.45
Degree level education	Women only	46,660	OR: 0.82 (0.80, 0.84)	$<1 \times 10^{-15}$	OR: 0.93 (0.79, 1.10)	0.41
Have a skilled job	All	67,684	OR: 0.87 (0.85, 0.89)	$<1 \times 10^{-15}$	OR: 0.95 (0.80, 1.13)	0.54
Have a skilled job	Men only	33,104	OR: 0.87 (0.85, 0.90)	$<1 \times 10^{-15}$	OR: 1.04 (0.81, 1.33)	0.76
Have a skilled job	Women only	34,580	OR: 0.86 (0.84, 0.89)	$<1 \times 10^{-15}$	OR: 0.88 (0.69, 1.12)	0.30
In employment	All	65,298	OR: 1.00 (0.94, 1.06)	0.97	OR: 0.77 (0.49, 1.21)	0.26
In employment	Men only	32,387	OR: 1.12 (1.05, 1.21)	0.0013	OR: 0.74 (0.43, 1.27)	0.28
In employment	Women only	32,911	OR: 0.77 (0.70, 0.86)	1×10^{-6}	OR: 0.87 (0.40, 1.87)	0.71
Social support measures						
Weekly visits from friends and family	All	87,750	OR: 1.09 (1.07, 1.11)	$<1 \times 10^{-15}$	OR: 0.91 (0.79, 1.05)	0.19
Weekly visits from friends and family	Men only	40,971	OR: 1.13 (1.11, 1.16)	$<1 \times 10^{-15}$	OR: 0.87 (0.72, 1.05)	0.14
Weekly visits from friends and family	Women only	46,779	OR: 1.04 (1.01, 1.07)	0.003	OR: 0.96 (0.77, 1.18)	0.68
Weekly participation in leisure and social activities	All	88,115	OR: 0.94 (0.92, 0.95)	3×10^{-15}	OR: 1.00 (0.88, 1.14)	0.99

Weekly participation in leisure and social activities	Men only	41,170	OR: 1.01 (0.99, 1.03)	0.39	OR: 0.99 (0.83, 1.18)	0.90
Weekly participation in leisure and social activities	Women only	46,945	OR: 0.87 (0.86, 0.89)	$<1 \times 10^{-15}$	OR: 1.00 (0.84, 1.21)	0.96
Weekly confiding in close friend or relative	All	85,887	OR: 0.99 (0.97, 1.00)	0.15	OR: 1.02 (0.89, 1.17)	0.77
Weekly confiding in close friend or relative	Men only	40,036	OR: 1.00 (0.98, 1.02)	0.92	OR: 0.96 (0.80, 1.15)	0.65
Weekly confiding in close friend or relative	Women only	45,851	OR: 0.98 (0.95, 1.00)	0.08	OR: 1.11 (0.90, 1.37)	0.34
Cohabitation with partner or spouse	All	80,782	OR: 1.03 (1.01, 1.05)	0.004	OR: 1.00 (0.85, 1.18)	0.99
Cohabitation with partner or spouse	Men only	38,698	OR: 1.13 (1.10, 1.16)	1×10^{-15}	OR: 1.06 (0.84, 1.33)	0.65
Cohabitation with partner or spouse	Women only	42,084	OR: 0.96 (0.93, 0.99)	0.004	OR: 0.96 (0.90, 1.37)	0.74

Supplementary Table S8: results from non-linear MR across deciles of IV-free BMI

Outcome	Individuals	Decile	Beta	Standard error	P value	BMI range within the decile
TDI	All	1	-0.047	0.009	6x10 ⁻⁸	12.0 to 22.0 kg/m ²
TDI	All	2	0.003	0.008	0.75	22.0 to 23.5 kg/m ²
TDI	All	3	-0.001	0.008	0.87	23.5 to 24.6 kg/m ²
TDI	All	4	0.014	0.008	0.09	26.4 to 25.7 kg/m ²
TDI	All	5	0.036	0.008	2x10 ⁻⁵	25.7 to 26.7 kg/m ²
TDI	All	6	0.016	0.008	0.05	26.7 to 27.8 kg/m ²
TDI	All	7	0.046	0.008	5x10 ⁻⁸	27.8 to 29.1 kg/m ²
TDI	All	8	0.017	0.009	0.043	29.1 to 30.7 kg/m ²
TDI	All	9	0.009	0.009	0.28	30.7 to 33.4 kg/m ²
TDI	All	10	0.040	0.009	5x10 ⁻⁶	33.4 to 74.7 kg/m ²
TDI	Men only	1	-0.064	0.014	4x10 ⁻⁶	12.0 to 22.0 kg/m ²
TDI	Men only	2	-0.008	0.013	0.567	22.0 to 23.5 kg/m ²
TDI	Men only	3	-0.009	0.013	0.49	23.5 to 24.6 kg/m ²
TDI	Men only	4	0.012	0.013	0.35	26.4 to 25.7 kg/m ²
TDI	Men only	5	0.025	0.013	0.06	25.7 to 26.7 kg/m ²
TDI	Men only	6	0.009	0.013	0.51	26.7 to 27.8 kg/m ²
TDI	Men only	7	0.061	0.013	4x10 ⁻⁶	27.8 to 29.1 kg/m ²
TDI	Men only	8	0.015	0.013	0.26	29.1 to 30.7 kg/m ²
TDI	Men only	9	0.020	0.013	0.14	30.7 to 33.4 kg/m ²
TDI	Men only	10	0.040	0.014	0.003	33.4 to 74.7 kg/m ²
TDI	Women only	1	-0.031	0.011	0.007	12.0 to 22.0 kg/m ²

TDI	Women only	2	0.002	0.011	0.85	22.0 to 23.5 kg/m ²
TDI	Women only	3	0.012	0.011	0.27	23.5 to 24.6 kg/m ²
TDI	Women only	4	0.013	0.011	0.22	26.4 to 25.7 kg/m ²
TDI	Women only	5	0.043	0.011	1x10 ⁻⁴	25.7 to 26.7 kg/m ²
TDI	Women only	6	0.028	0.011	0.010	26.7 to 27.8 kg/m ²
TDI	Women only	7	0.048	0.011	1x10 ⁻⁵	27.8 to 29.1 kg/m ²
TDI	Women only	8	0.006	0.011	0.60	29.1 to 30.7 kg/m ²
TDI	Women only	9	0.013	0.011	0.27	30.7 to 33.4 kg/m ²
TDI	Women only	10	0.030	0.011	0.009	33.4 to 74.7 kg/m ²
Income	All	1	0.066	0.010	2x10 ⁻¹⁰	12.0 to 22.0 kg/m ²
Income	All	2	0.023	0.010	0.022	22.0 to 23.5 kg/m ²
Income	All	3	-0.013	0.010	0.20	23.5 to 24.6 kg/m ²
Income	All	4	-0.023	0.010	0.019	26.4 to 25.7 kg/m ²
Income	All	5	-0.034	0.010	0.0006	25.7 to 26.7 kg/m ²
Income	All	6	-0.028	0.010	0.005	26.7 to 27.8 kg/m ²
Income	All	7	-0.033	0.010	0.0008	27.8 to 29.1 kg/m ²
Income	All	8	-0.019	0.010	0.05	29.1 to 30.7 kg/m ²
Income	All	9	-0.020	0.010	0.040	30.7 to 33.4 kg/m ²
Income	All	10	-0.031	0.010	0.001	33.4 to 74.7 kg/m ²
Income	Men only	1	0.094	0.016	4x10 ⁻⁹	12.0 to 22.0 kg/m ²
Income	Men only	2	0.024	0.016	0.13	22.0 to 23.5 kg/m ²
Income	Men only	3	-0.012	0.016	0.45	23.5 to 24.6 kg/m ²
Income	Men only	4	-0.007	0.015	0.63	26.4 to 25.7 kg/m ²
Income	Men only	5	-0.016	0.016	0.30	25.7 to 26.7 kg/m ²
Income	Men only	6	-0.036	0.016	0.021	26.7 to 27.8 kg/m ²

Income	Men only	7	-0.021	0.016	0.17	27.8 to 29.1 kg/m ²
Income	Men only	8	-0.031	0.015	0.040	29.1 to 30.7 kg/m ²
Income	Men only	9	-0.021	0.016	0.18	30.7 to 33.4 kg/m ²
Income	Men only	10	-0.042	0.016	0.007	33.4 to 74.7 kg/m ²
Income	Women only	1	0.051	0.014	0.0002	12.0 to 22.0 kg/m ²
Income	Women only	2	0.004	0.013	0.76	22.0 to 23.5 kg/m ²
Income	Women only	3	-0.009	0.013	0.49	23.5 to 24.6 kg/m ²
Income	Women only	4	-0.030	0.013	0.019	26.4 to 25.7 kg/m ²
Income	Women only	5	-0.042	0.013	0.001	25.7 to 26.7 kg/m ²
Income	Women only	6	-0.041	0.013	0.001	26.7 to 27.8 kg/m ²
Income	Women only	7	-0.036	0.013	0.005	27.8 to 29.1 kg/m ²
Income	Women only	8	-0.008	0.013	0.54	29.1 to 30.7 kg/m ²
Income	Women only	9	-0.009	0.013	0.47	30.7 to 33.4 kg/m ²
Income	Women only	10	-0.033	0.012	0.007	33.4 to 74.7 kg/m ²
Cohabitation	All	1	0.073	0.018	7x10 ⁻⁵	12.0 to 22.0 kg/m ²
Cohabitation	All	2	0.076	0.019	7x10 ⁻⁵	22.0 to 23.5 kg/m ²
Cohabitation	All	3	0.036	0.019	0.06	23.5 to 24.6 kg/m ²
Cohabitation	All	4	0.008	0.020	0.69	26.4 to 25.7 kg/m ²
Cohabitation	All	5	-0.015	0.020	0.45	25.7 to 26.7 kg/m ²
Cohabitation	All	6	-0.013	0.020	0.52	26.7 to 27.8 kg/m ²
Cohabitation	All	7	-0.016	0.020	0.40	27.8 to 29.1 kg/m ²
Cohabitation	All	8	-0.027	0.019	0.16	29.1 to 30.7 kg/m ²
Cohabitation	All	9	-0.034	0.019	0.07	30.7 to 33.4 kg/m ²
Cohabitation	All	10	-0.071	0.017	5x10 ⁻⁵	33.4 to 74.7 kg/m ²
Cohabitation	Men only	1	0.183	0.027	1x10 ⁻¹¹	12.0 to 22.0 kg/m ²

Cohabitation	Men only	2	0.068	0.029	0.020	22.0 to 23.5 kg/m ²
Cohabitation	Men only	3	0.096	0.030	0.002	23.5 to 24.6 kg/m ²
Cohabitation	Men only	4	0.050	0.031	0.10	26.4 to 25.7 kg/m ²
Cohabitation	Men only	5	-0.012	0.031	0.71	25.7 to 26.7 kg/m ²
Cohabitation	Men only	6	-0.015	0.031	0.63	26.7 to 27.8 kg/m ²
Cohabitation	Men only	7	0.004	0.031	0.89	27.8 to 29.1 kg/m ²
Cohabitation	Men only	8	-0.044	0.030	0.15	29.1 to 30.7 kg/m ²
Cohabitation	Men only	9	0.006	0.030	0.83	30.7 to 33.4 kg/m ²
Cohabitation	Men only	10	-0.047	0.027	0.08	33.4 to 74.7 kg/m ²
Cohabitation	Women only	1	0.022	0.025	0.38	12.0 to 22.0 kg/m ²
Cohabitation	Women only	2	0.046	0.026	0.08	22.0 to 23.5 kg/m ²
Cohabitation	Women only	3	0.035	0.026	0.17	23.5 to 24.6 kg/m ²
Cohabitation	Women only	4	-0.031	0.026	0.22	26.4 to 25.7 kg/m ²
Cohabitation	Women only	5	-0.011	0.025	0.65	25.7 to 26.7 kg/m ²
Cohabitation	Women only	6	-0.023	0.025	0.35	26.7 to 27.8 kg/m ²
Cohabitation	Women only	7	-0.028	0.025	0.26	27.8 to 29.1 kg/m ²
Cohabitation	Women only	8	-0.045	0.025	0.07	29.1 to 30.7 kg/m ²
Cohabitation	Women only	9	-0.050	0.024	0.037	30.7 to 33.4 kg/m ²
Cohabitation	Women only	10	-0.085	0.023	0.0002	33.4 to 74.7 kg/m ²

Supplementary Table S9: Summary of the results from the non-linear Mendelian randomisation analyses for all outcome traits against BMI

				Evidence of non-linearity from Fractional Polynomial model		Evidence of non-linearity from Piecewise Linear model	
Outcome	Strata	Number	IV P-value from the Fractional Polynomial model	Fractional polynomial test	Cochran Q test	Quadratic test	Cochran Q
Socioeconomic position measures							
Townsend deprivation index	All	377,786	<1x10 ⁻¹⁵	0.00028	7x10 ⁻⁸	3x10 ⁻⁹	2x10 ⁻¹⁴
Townsend deprivation index	Men only	174,144	5x10 ⁻¹²	0.016	1x10 ⁻⁵	2x10 ⁻⁷	2x10 ⁻⁸
Townsend deprivation index	Women only	203,642	7x10 ⁻⁸	0.021	0.01	0.006	3x10 ⁻⁵
Annual household income	All	326,117	<1x10 ⁻¹⁵	0.0006	8x10 ⁻¹³	4x10 ⁻⁹	5x10 ⁻¹⁵
Annual household income	Men only	156,521	1x10 ⁻¹⁵	0.04	3x10 ⁻⁸	2x10 ⁻⁹	5x10 ⁻⁹
Annual household income	Women only	169,596	8x10 ⁻¹⁰	0.02	0.003	0.004	5x10 ⁻⁶
Years in education	All	374,658	0.0001	0.48	0.34	0.13	0.22

Years in education	Men only	172,637	0.0004	0.99	0.54	0.96	0.44
Years in education	Women only	202,021	0.02	0.14	0.88	0.031	0.25
Degree level education	All	374,658	2x10 ⁻⁵	0.13	0.68	0.07	0.53
Degree level education	Men only	172,637	0.001	0.73	0.06	0.82	0.04
Degree level education	Women only	202,021	0.005	0.09	0.14	0.05	0.34
Have a skilled job	All	245,138	0.0031	0.53	0.79	0.49	0.26
Have a skilled job	Men only	117,866	0.005	0.14	0.5	0.16	0.3
Have a skilled job	Women only	127,272	0.04	0.87	0.28	0.72	0.41
In employment*	All	222,288					
In employment*	Men only	109,002					
In employment*	Women only	113,286					
Social support measures							
Weekly visits from friends and family	All	375,985	0.034	0.06	0.034	0.035	0.1
Weekly visits from friends and family	Men only	173,165	0.33	0.33	0.042	0.058	0.42
Weekly visits from friends and family	Women only	202,820	0.077	0.13	0.5	0.31	0.43

Weekly participation in leisure and social activities	All	377,246	0.001	0.001	1×10^{-7}	4×10^{-10}	2×10^{-11}
Weekly participation in leisure and social activities	Men only	173,923	0.014	0.044	0.14	4×10^{-6}	1×10^{-5}
Weekly participation in leisure and social activities	Women only	203,323	0.003	0.003	0.009	2×10^{-5}	1×10^{-6}
Weekly confiding in close friend or relative	All	367,216	0.098	0.12	0.08	0.19	0.14
Weekly confiding in close friend or relative	Men only	168,707	0.097	0.12	0.32	0.13	0.035
Weekly confiding in close friend or relative	Women only	198,509	0.46	0.52	0.65	0.63	0.94
Cohabitation with partner or spouse	All	347,329	1×10^{-5}	2×10^{-5}	0.0005	1×10^{-12}	2×10^{-9}

Cohabitation with partner or spouse	Men only	163,873	1×10^{-11}	4×10^{-8}	0.0009	4×10^{-13}	4×10^{-9}
Cohabitation with partner or spouse	Women only	183,456	0.0003	0.003	0.024	7×10^{-6}	0.003

*Greyed out as no results available because the outcome is very unbalanced which meant the models were unable to run

Supplementary Table S10. Results of within-family analyses compared to MR in unrelated individuals

Outcome	Strata	Type of analysis	Number	Difference in outcome (95% CI) per SD higher BMI*	P value
Townsend deprivation index	All	MR in unrelated individuals	379209	0.079 (0.055, 0.103)	7x10 ⁻¹¹
Townsend deprivation index	All	Siblings [Non-genetic, family effects]	39865	0.047 (0.031, 0.062)	3x10 ⁻⁹
Townsend deprivation index	All	Siblings [MR, family effects]	39865	0.021 (-0.136, 0.178)	0.79
Townsend deprivation index	Men only	MR in unrelated individuals	174059	0.077 (0.039, 0.116)	0.00008
Townsend deprivation index	Men only	Siblings [Non-genetic, family effects]	16777	-0.006 (-0.045, 0.034)	0.78
Townsend deprivation index	Men only	Siblings [MR, family effects]	16777	-0.135 (-0.525, 0.254)	0.50
Townsend deprivation index	Women only	MR in unrelated individuals	205150	0.081 (0.051, 0.111)	1x10 ⁻⁷
Townsend deprivation index	Women only	Siblings [Non-genetic, family effects]	23088	0.078 (0.054, 0.101)	5x10 ⁻⁷
Townsend deprivation index	Women only	Siblings [MR, family effects]	23088	0.234 (-0.006, 0.474)	0.06
Annual household income	All	MR in unrelated individuals	327244	-0.067 (-0.093, -0.042)	1x10 ⁻⁷
Annual household income	All	Siblings [Non-genetic, family effects]	34523	-0.027 (-0.043, -0.011)	0.001
Annual household income	All	Siblings [MR, family effects]	34523	0.112 (-0.059, 0.283)	0.20
Annual household income	Men only	MR in unrelated individuals	156467	-0.044 (-0.084, -0.004)	0.029
Annual household income	Men only	Siblings [Non-genetic, family effects]	15172	0.015 (-0.024, 0.055)	0.45
Annual household income	Men only	Siblings [MR, family effects]	15172	0.364 (-0.076, 0.804)	0.11
Annual household income	Women only	MR in unrelated individuals	170777	-0.085 (-0.118, -0.053)	2x10 ⁻⁷
Annual household income	Women only	Siblings [Non-genetic, family effects]	19351	-0.042 (-0.068, -0.017)	0.001
Annual household income	Women only	Siblings [MR, family effects]	19351	-0.039 (-0.282, 0.204)	0.75
Years in education	All	MR in unrelated individuals	375950	-0.047 (-0.071, -0.022)	0.0002
Years in education	All	Siblings [Non-genetic, family effects]	39570	-0.028 (-0.044, -0.012)	0.0007
Years in education	All	Siblings [MR, family effects]	39570	-0.009 (-0.171, 0.154)	0.91

Years in education	Men only	MR in unrelated individuals	172486	-0.055 (-0.094, -0.015)	0.020
Years in education	Men only	Siblings [Non-genetic, family effects]	16640	-0.070 (-0.111, -0.029)	0.0007
Years in education	Men only	Siblings [MR, family effects]	16640	0.010 (-0.377, 0.398)	0.96
Years in education	Women only	MR in unrelated individuals	203464	-0.041 (-0.072, 0.010)	0.010
Years in education	Women only	Siblings [Non-genetic, family effects]	22930	-0.015 (-0.040, 0.009)	0.22
Years in education	Women only	Siblings [MR, family effects]	22930	-0.020 (-0.265, 0.225)	0.87
Degree	All	MR in unrelated individuals	375950	-0.082 (-0.134, -0.030)	0.0002
Degree	All	Siblings [Non-genetic, family effects]	39335	-0.047 (-0.081, -0.014)	0.006
Degree	All	Siblings [MR, family effects]	39335	-0.029 (-0.381, 0.323)	0.87
Degree	Men only	MR in unrelated individuals	172486	-0.085 (-0.168, -0.003)	0.043
Degree	Men only	Siblings [Non-genetic, family effects]	8007	-0.072 (-0.156, 0.013)	0.10
Degree	Men only	Siblings [MR, family effects]	8007	-0.166 (-0.968, 0.637)	0.69
Degree	Women only	MR in unrelated individuals	203464	-0.080 (-0.147, -0.013)	0.019
Degree	Women only	Siblings [Non-genetic, family effects]	14346	-0.033 (-0.086, 0.020)	0.22
Degree	Women only	Siblings [MR, family effects]	14346	-0.058 (-0.615, 0.499)	0.84
Have a skilled job	All	MR in unrelated individuals	246844	-0.144 (-0.224, -0.064)	0.0004
Have a skilled job	All	Siblings [Non-genetic, family effects]	25609	0.007 (-0.048, 0.061)	0.81
Have a skilled job	All	Siblings [MR, family effects]	25609	0.342 (-0.205, 0.890)	0.22
Have a skilled job	Men only	MR in unrelated individuals	118302	-0.182 (-0.314, -0.049)	0.007
Have a skilled job	Men only	Siblings [Non-genetic, family effects]	5474	0.012 (-0.127, 0.151)	0.86
Have a skilled job	Men only	Siblings [MR, family effects]	5474	0.160 (-1.17, 1.49)	0.81
Have a skilled job	Women only	MR in unrelated individuals	128542	-0.119 (-0.219, -0.019)	0.02
Have a skilled job	Women only	Siblings [Non-genetic, family effects]	9081	0.002 (-0.081, 0.086)	0.96
Have a skilled job	Women only	Siblings [MR, family effects]	9081	-0.015 (-0.822, 0.792)	0.97

In employment	All	MR in unrelated individuals	223821	-0.039 (-0.232, 0.153)	0.69
In employment	All	Siblings [Non-genetic, family effects]	23722	-0.082 (-0.238, 0.075)	0.31
In employment	All	Siblings [MR, family effects]	23722	0.593 (-0.757, 1.944)	0.39
In employment	Men only	MR in unrelated individuals	109421	-0.060 (-0.322, 0.201)	0.65
In employment	Men only	Siblings [Non-genetic, family effects]	5114	0.110 (-0.213, 0.433)	0.50
In employment	Men only	Siblings [MR, family effects]	5114	1.794 (-0.709, 4.297)	0.16
In employment	Women only	MR in unrelated individuals	114400	0.007 (-0.296, 0.309)	0.97
In employment	Women only	Siblings [Non-genetic, family effects]	8245	-0.239 (-0.533, 0.055)	0.11
In employment	Women only	Siblings [MR, family effects]	8245	-0.214 (-2.435, 2.007)	0.85
Weekly visits from friends and family	All	MR in unrelated individuals	377321	-0.011 (-0.074, 0.051)	0.72
Weekly visits from friends and family	All	Siblings [Non-genetic, family effects]	39477	0.049 (0.004, 0.093)	0.034
Weekly visits from friends and family	All	Siblings [MR, family effects]	39477	-0.208 (-0.664, 0.248)	0.37
Weekly visits from friends and family	Men only	MR in unrelated individuals	173044	-0.045 (-0.137, 0.048)	0.34
Weekly visits from friends and family	Men only	Siblings [Non-genetic, family effects]	8032	0.095 (-0.007, 0.196)	0.07
Weekly visits from friends and family	Men only	Siblings [MR, family effects]	8032	0.204 (-0.743, 1.151)	0.67
Weekly visits from friends and family	Women only	MR in unrelated individuals	204277	0.018 (-0.068, 0.104)	0.69
Weekly visits from friends and family	Women only	Siblings [Non-genetic, family effects]	14417	0.017 (-0.061, 0.096)	0.67
Weekly visits from friends and family	Women only	Siblings [MR, family effects]	14417	0.532 (-0.279, 1.343)	0.20
Weekly participation in leisure and social activities	All	MR in unrelated individuals	378615	-0.057 (-0.112, -0.002)	0.044
Weekly participation in leisure and social activities	All	Siblings [Non-genetic, family effects]	39561	-0.053 (-0.090, -0.015)	0.01
Weekly participation in leisure and social activities	All	Siblings [MR, family effects]	39561	0.063 (-0.313, 0.438)	0.74
Weekly participation in leisure and social activities	Men only	MR in unrelated individuals	173796	-0.076 (-0.164, 0.012)	0.09
Weekly participation in leisure and social activities	Men only	Siblings [Non-genetic, family effects]	8065	0.006 (-0.087, 0.098)	0.90

Weekly participation in leisure and social activities	Men only	Siblings [MR, family effects]	8065	0.486 (-0.397, 1.369)	0.28
Weekly participation in leisure and social activities	Women only	MR in unrelated individuals	204819	-0.044 (-0.115, 0.027)	0.23
Weekly participation in leisure and social activities	Women only	Siblings [Non-genetic, family effects]	14426	-0.098 (-0.157, -0.039)	0.001
Weekly participation in leisure and social activities	Women only	Siblings [MR, family effects]	14426	-0.012 (-0.594, 0.571)	0.97
Weekly confiding in close friend or relative	All	MR in unrelated individuals	368555	0.010 (-0.049, 0.070)	0.73
Weekly confiding in close friend or relative	All	Siblings [Non-genetic, family effects]	38511	-0.019 (-0.059, 0.021)	0.35
Weekly confiding in close friend or relative	All	Siblings [MR, family effects]	38511	-0.120 (-0.514, 0.274)	0.55
Weekly confiding in close friend or relative	Men only	MR in unrelated individuals	168649	0.026 (-0.064, 0.116)	0.58
Weekly confiding in close friend or relative	Men only	Siblings [Non-genetic, family effects]	7796	0.033 (-0.06, 0.127)	0.49
Weekly confiding in close friend or relative	Men only	Siblings [MR, family effects]	7796	-1.068 (-1.93, -0.211)	0.015
Weekly confiding in close friend or relative	Women only	MR in unrelated individuals	199906	-0.001 (-0.081, 0.079)	0.98
Weekly confiding in close friend or relative	Women only	Siblings [Non-genetic, family effects]	14092	-0.021 (-0.087, 0.046)	0.54
Weekly confiding in close friend or relative	Women only	Siblings [MR, family effects]	14092	0.098 (-0.559, 0.756)	0.77
Cohabitation with partner or spouse	All	MR in unrelated individuals	348570	-0.067 (-0.135, 0.002)	0.06
Cohabitation with partner or spouse	All	Siblings [Non-genetic, family effects]	35735	-0.062 (-0.108, -0.017)	0.01
Cohabitation with partner or spouse	All	Siblings [MR, family effects]	35735	-0.049 (-0.480, 0.382)	0.82
Cohabitation with partner or spouse	Men only	MR in unrelated individuals	163828	0.094 (-0.017, 0.205)	0.10
Cohabitation with partner or spouse	Men only	Siblings [Non-genetic, family effects]	7460	0.088 (-0.031, 0.207)	0.15
Cohabitation with partner or spouse	Men only	Siblings [MR, family effects]	7460	0.077 (0.002, 0.152)	0.045
Cohabitation with partner or spouse	Women only	MR in unrelated individuals	184742	-0.173 (-0.261, -0.086)	0.00009
Cohabitation with partner or spouse	Women only	Siblings [Non-genetic, family effects]	12705	-0.094 (-0.165, -0.023)	0.009

Cohabitation with partner or spouse	Women only	Siblings [MR, family effects]	12705	-0.628 (-1.288, 0.032)	0.06
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